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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
SOUAYA, JEHANNE E

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 11/21/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/027,439	Portugal et al
Examiner	**Art Unit**
Jehanne Souaya	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jun 12, 2002* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *21-39 and 45-52* is/are pending in the application.

4a) Of the above, claim(s) *21-36* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *37-39 and 45-52* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☒ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 13
4) ☒ Interview Summary (PTO-413) Paper No(s). 21
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Please note that the art unit designation for the examiner has been changed from 1655 to 1634.

1. Currently, claims 37-39 and 45-52 are pending in the instant application. The response filed Jun 12, 2002 states that claims 45-56 have been added, however the examiner could not find claims 53-56 in the response, therefore, it is assumed that mention of claims 53-56 is in error. An action on the merits of claims 37-39 and 45-52 follows. Claims 21-36 have been withdrawn from consideration as being directed to nonelected subject matter. All the amendments and arguments have been thoroughly reviewed but are deemed insufficient to place this application in condition for allowance. Any rejections not reiterated are hereby withdrawn. The following objections and rejections are newly applied. They constitute the complete set being presently applied to the instant Application. This action is NON-FINAL.

Specification

2. The disclosure is objected to because of the following: Table 2, which was amended January 21, 1999, lists sequences that have not been identified by SEQ ID NO. Each entry in the table is required to be identified by a SEQ ID NO, even if some of the entries have identical SEQ ID NOS. For example, the fourth entry in the table does not have a SEQ ID NO. Although it is identical to SEQ ID NO 23, it should be identified by SEQ ID NO 23 as well. See 37 CFR1.821(d), MPEP section 2422. Appropriate correction is required.

Claim Objections

3. Claims 38-39, 45 and 46 are objected to because the claims refer to nucleic acid sequences in a table when they can be designated by SEQ ID NO in the claim.

MPEP 2173(s) states "Where possible, claims are to be complete in themselves. Incorporation by reference to a specific figure or table "is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than duplicating a drawing or table into the claim. Incorporation by reference is a necessity doctrine, not for applicant's convenience."

In the instant application, it appears that the claims can practically refer to the nucleic acids in table 2 using SEQ ID NOS. Appropriate correction is required.

Claim Rejections - 35 USC § 101

4. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claims 37-39, 45, 46, 49, 50 and 51 rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The specification does not define the term 'consisting essentially of' or what is 'essential' to the claimed nucleic acid molecules. This language has been interpreted broadly as "open" language (for example: 'comprising') and therefore, the recitation of 'a nucleic acid molecule", without the recitation of the word "isolated" is directed to a product of nature, which is non-statutory subject matter. This rejection can be overcome by reciting instead "an isolated nucleic acid molecule".

Claim Rejections - 35 USC § 112

Enablement

6. Claims 37-39 and 45-52 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims, reciting language such as "complementary" (all claims), "sequences of nucleotides in Table 2" (claims 38-39, 45-46), and "consisting essentially of" or "comprising a nucleotide sequence as set forth *in*" (claims 47-51) are broadly drawn to variants and homologs of the claimed sequences, from any source. With regard to the term "complementary", the specification defines such as "nucleic acid sequences which are substantially complementary or as defined as being capable of hybridizing to the nucleic acid segment of said sequences under relatively stringent conditions", however the specification does not define what is encompassed by "substantially complementary" or "relatively stringent conditions", such that the skilled artisan could identify the broadly claimed sequences from any sequence, other than by SEQ ID NO, without undue experimentation. With regard to the recitation of "sequences in Table 2", the specification sets forth a table and only specifies 30-40 nucleotides for each entry in the table, however, as the claim is written, it broadly encompasses sequences comprising only 10 sequential nucleotides from any of the sequences in table 2, as well as a whole genome or a complete rDNA or rRNA sequence from any source. For example, the claims encompass the

entire genome of S. Flexneri French strain, which has not been taught in the specification. The specification does not teach where to obtain S. Flexneri French strain, does not provide any deposit information for this strain (as well as a number of others from the table), nor does the specification teach how this strain differs from other S. Flexneri strains. With regard to the recitation of "set forth in" the specification does not define how many nucleotides "in" the specific sequences are present, therefore this recitation has been broadly interpreted to encompass any sequence that comprises as little as a single nucleotide from the recited SEQ ID NOS. As stated previously, such sequences encompass mutants, allelic variants, and homologs, from any source, as well as unknown and undisclosed sequences that have not been taught or described by the specification. The specification has not defined the recitation of the terms in question such the skilled artisan would be able to establish a predictable correlation between the structure of the specifically recited sequences and the sequences of the large number of mutants, variants, and homologs encompassed by the broadly claimed invention, without undue experimentation.

Written Description

7. Claims 37-39 and 45-52 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims, reciting language such as "complementary" (all claims), "sequences of nucleotides in Table 2" (claims 38-39, 45-46), and "consisting essentially of" or "comprising a

nucleotide sequence as set forth *in*" (claims 47-51) are broadly drawn to variants and homologs of the claimed sequences, from any source. With regard to the term "complementary", the specification defines (p. 14, para 2) such as "nucleic acid sequences which are substantially complementary or as defined as being capable of hybridizing to the nucleic acid segment of said sequences under relatively stringent conditions", however the specification does not define what is encompassed by "substantially complementary" or "relatively stringent conditions" such that the skilled artisan could identify the broadly claimed sequences from any sequence, other than by SEQ ID NO. With regard to the recitation of "sequences in Table 2", the specification sets forth a table and only specifies 30-40 nucleotides for each entry in the table, however, as the claim is written, it broadly encompasses sequences comprising only 10 sequential nucleotides from any of the sequences in table 2, including a complete rDNA or rRNA sequence from any source or an entire genome, for example, the entire genome of S. Flexneri French strain, which has not been taught in the specification. The specification does not teach where to obtain S. Flexneri French strain, does not provide any deposit information for this strain (as well as a number of other strains from the table), nor does the specification teach how this strain differs from other S. Flexneri strains. With regard to the recitation of "set forth in" the specification does not define how many nucleotides "in" the specific sequences are present, therefore this recitation has been broadly interpreted to encompass any sequence that comprises as little as a single nucleotide from the recited SEQ ID NOS. As stated previously, such sequences encompass mutants, allelic variants, and homologs, from any source, as well as unknown sequences that have not been

taught or described by the specification. The specification has not defined the terms in question sufficiently to allow the skilled artisan to establish a correlation between the structure of the specifically recited sequences and the sequences of the large genus of mutants, variants, and homologs, from any source, encompassed by the broadly claimed invention. Therefore, the disclosed structural feature does not constitute a substantial portion of the claimed genus of nucleic acid molecules.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NOS: 3-7, and 9-17, or the specific nucleotide changes recited in the claims, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993), and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims

directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

Accordingly, the specification does not provide a written description of the invention of claims 37-39, and 45-52.

Indefinite

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 37-39, and 45-52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 37-39 and 45-46 are indefinite in the recitation of "E. Coli equivalent position of SEQ ID NO 7". Since SEQ ID NO 7 is an E. Coli sequence, it is unclear what is encompassed by an "E. Coli equivalent position". It is unclear if the claims are drawn to only E. Coli nucleic acids.

B) Claims 38-39 and 45-46 are indefinite in the recitation of "sequences of nucleotides in Table 2" as it is unclear if the claim refers only to specific SEQ ID NOS from table 2, any sequence comprising as few as 10 sequential nucleotides from any of the sequences in table 2, or to a whole genome or rDNA or rRNA sequence from the selected strains of microorganisms recited in the table. It is noted that the term "consisting essentially of" is being interpreted as "open" language (that is, "comprising") because the specification does not define how many extra nucleotides, other than those identified by SEQ ID NO, are encompassed by the recitation of "consisting essentially". The specification does not define what is considered 'essential' to the claimed nucleic acid sequences.

C) Claims 47-51 are indefinite in the recitation of "as set forth in" because it is unclear how many nucleotides of the recited SEQ ID NOS must be present in the claimed nucleic acid molecules. As the specification does not define this term, the metes and bounds of the claim are unclear.

D) Claim 50 is indefinite in the recitation of "sequential nucleotides" because it is unclear if the claim encompasses a molecule which only must contain as little as two sequential nucleotides from any of the recited SEQ ID NOS or to a nucleic acid that contains sequentially,

any number of the recited SEQ ID NOS. Since the specification does not define this recitation, the metes and bounds of the claim are unclear.

E) Claims 37-39 and 45-52 lack sufficient antecedent basis for the recitation of "said molecule" or "said isolated molecule" because the claims instead recite "nucleic acid molecule". This rejection can be easily overcome by reciting instead 'the molecule' or 'the isolated molecule', or inserting the term 'nucleic acid' between 'said" and "molecule" or between "said" and "isolated molecule".

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Applicant should note that the following terms and recitations have been interpreted broadly in the following rejections under 35 USC 102 and 103.

A) "consisting essentially of" has been interpreted as 'open' language (ie: comprising). The specification does not teach the length of a nucleic acid that is encompassed by "consisting

essentially of" nor does the specification the specification teach what is 'essential' to the claimed nucleic acid sequences.

B) "complementary" has been interpreted to mean two nucleic acids that have any number of complementary nucleotides in common, or are capable of hybridizing to each other under any conditions. The specification defines (p. 14, para 2) "complementary" as "nucleic acid sequences which are substantially complementary or as defined as being capable of hybridizing to the nucleic acid segment of said sequences under relatively stringent conditions", however the specification does not define what is encompassed by "substantially complementary" or "relatively stringent conditions". Therefore, the recitation has been interpreted in it's broadest sense.

C) "sequences of nucleotides in Table 2" has been broadly interpreted to mean sequences that contain as few as 10 sequential nucleotides from the sequences recited in table 2 with the alterations indicated in the claims.

D) "set forth in" has been broadly interpreted to mean a sequence that can have a single nucleotide in common with the recited SEQ ID NOS. Neither the specification nor the claims make clear how many nucleotides are encompassed by such recitation.

E) "sequential nucleotides" in claim 50 has been interpreted to encompass nucleic acid molecules containing at least two sequential nucleotides from the recited SEQ ID NOS because the claim does not make clear how many "sequential nucleotides" must be present in the claimed nucleic acid molecule.

11. Claims 37, 49 and 50 are rejected under 35 U.S.C. 102(a) as being anticipated by accession numbers X80679, X80729, X80678, and X80730 (2/20/1996, accession number provided in Cilia et al).

Accession number X80679 teaches a sequences that comprises SEQ ID NO 9, accession number X80729 teaches a sequence that comprises SEQ ID NO 10, accession number X80678 teaches a sequence that comprises SEQ ID NO 12, and accession number X80730 teaches a sequence that comprises SEQ ID NO 16, and SEQ ID NO 24 (which contains an insertion of a T between positions 88 and 89 of an equivalent sequence in SEQ ID NO 7). It is noted that "consisting essentially of" in claim 50 has been interpreted broadly as 'open' language.

12. Claim 37 and 49-50 are rejected under 35 U.S.C. 102(b) as being anticipated by accession number J014695 (April 15, 1994).

It is noted that "consisting essentially of" has been interpreted as 'open' language. J014695 teaches a sequence of 7508 nucleotides which contains a sequence that is identical to a nucleic acid molecule that contains an insertion of a T between positions 88 and 89 of SEQ ID NO 7 (alignment provided). With respect to claims 49 and 50, accession number J014695 comprises sequences set forth *in* the claimed SEQ ID NOS.

13. Claims 49 and 50 rejected under 35 U.S.C. 102(b) as being anticipated by accession number A14565.

With respect to claims 49 and 50, accession number A14565 comprises sequences set forth *in* the claimed SEQ ID NOS.

14. Claims 49 and 50 are rejected under 35 U.S.C. 102(b) as being anticipated by accession number U18997 (December 30, 1994).

Accession number U18997 teaches a sequence that comprises the reverse complement of SEQ ID NO 10. Therefore, accession number U18997 inherently teaches a sequence that is completely complementary to SEQ ID NO 10.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 37-39, 45-48 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over accession number A14565 (September 29, 1994) in view of Dyson, N.J. (Essential Molecular Biology Vol. II: A Practical Approach, chapter 5, pages 111-156, Brown, T.A. ed. Oxford University Press, Oxford, 1992).

Accession number A14565 teaches a sequence of 16S rRNA from E. Coli. With respect to claims 37-39, 45, and 46: this sequence contains only a single nucleotide difference with respect to the nucleic acid molecules in the claims (it is noted that the sequence of accession number A14565 is identical to SEQ ID NO 7). Based on the broad interpretation of the term "complementary", the full complement of the sequence of accession number A14565 is considered "complementary" to the claimed nucleic acid molecules. With respect to claims 47 and 48, the sequence of accession number A14565 contains only 5 mismatches and a gap of 1 nucleotide with respect to the entirety of SEQ ID NO 3 (sequence alignment provided). Therefore, the full complement of accession number A14565 is also considered "complementary" to the claimed nucleic acid sequences. With respect to claim 52, the sequence of accession number A14565 contains only 7 mismatches, an extra nucleotide, and a single nucleotide gap with respect to the entirety of SEQ ID NO 6 (alignment provided). Although accession number A14565 does not teach the full complement of the sequence, it would have

been prima facie obvious to one of ordinary skill in the art to construct the full complement of accession number A14565 to obtain a probe that would hybridize to accession number A14565 for the purposes of detecting accession number A14565. Such methods were readily used in the art at the time of the invention, as exemplified by Dyson, which teaches constructing probes for the purposes of hybridization detection assays.

17. Claim 51 is rejected under 35 U.S.C. 103(a) as being unpatentable over Accession numbers A14565 and J014695, in view of Dyson and Ahern, Holly (The Scientist, July 1995, vol. 9, from the internet: pp 1-5).

Accession number J014695 comprises sequences set forth *in* the claimed SEQ ID NOS of claim 50. Accession number A14565 comprises sequences set forth *in* the claimed SEQ ID NOS of claim 50. Dyson teaches constructing probes for the purposes of hybridization detection assays. Although the accession numbers and Dyson do not teach the sequences in kit format, Ahern teaches that kits containing premade biochemicals and kits offer scientists the opportunity to better manage time (p. 4). Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to construct probes for the purposes of detecting the cited accession numbers for the purposes of detecting them in a sample. It would have been prima facie obvious to the ordinary artisan that probes comprising the full complement of the cited accession numbers could be used effectively to detect the accession numbers in a sample. It would further have been prima facie obvious to the ordinary artisan that packaging the

probes in kit format would have provided a convenient format to contain the probes for the purpose of detecting the 16S rRNA operon of E. Coli.

Conclusion

18. No claims are allowable, however allowable subject matter does exist. SEQ ID NOS 3-6 are free of the cited prior art.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Souaya whose telephone number is (703)308-6565. The examiner can normally be reached Monday-Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jehanne Souaya

Jehanne Souaya
Patent examiner
Art Unit 1634
11/14/2002